Amendments to the Claim:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1 (original). A method for preventing or arresting invasive remodelling in a mammal, the invasive remodelling not comprising contraction of tissue or corneal ulceration, the method comprising 1) inhibiting or abolishing, in the mammal, the in vivo protein cleaving actions of plasmin as well as of active derivatives thereof and 2) simultaneously therewith inhibiting or abolishing the in vivo protein cleaving actions of at least one proteolytic enzyme which is different from plasmin as well as from active derivatives thereof and which exerts its action on at least one extracellular protein on which plasmin and active derivatives of plasmin also act enzymatically, said at least one proteolytic enzyme being non-murine (including human) analogue(s) of murine metalloprotease(s) which, isolated or in combination, is/are essential for embryo implantation and/or wound healing in $Plg^{-/-}$ mice but not in wildtype mice, or which, isolated or in combination, is/are necessary for invasive tissue destruction associated with malignant growth in mice in which the protein cleaving actions of plasmin are substantially abolished.

2 (original). A method according to claim 1, wherein the in vivo protein cleaving actions of plasmin are substantially abolished.

3 (original). A method according to claim 1, wherein the in vivo protein cleaving actions of the at least one proteolytic enzyme are substantially abolished.

4 (currently amended). A method ~~for preventing or arresting invasive remodelling in a mammal, the invasive remodelling not comprising contraction of tissue or corneal ulceration, the method~~ according to claim 1 comprising administering, to the

mammal, an effective amount of a combination of 1) at least one first substance which, in the mammal, effects inhibition of the in vivo protein cleaving actions of plasmin as well as of active derivatives thereof, and 2) at least one second substance which, in the mammal, effects inhibition of the in vivo protein cleaving actions of at least one proteolytic enzyme which is different from plasmin as well as from active derivatives thereof and which exerts its action on at least one extracellular protein on which plasmin and active derivatives of plasmin also act enzymatically, said at least one second substance being at least one metalloprotease inhibitor which, upon administration in an effective amount, results in a significantly higher inhibition of embryo implantation and/or wound healing in $Plg^{-/-}$ mice than in wildtype mice, or results in abolition of invasive tissue destruction associated with malignant growth in mice in which the protein cleaving actions of plasmin are substantially abolished, the at least one first and second substances being administered either simultaneously or with such an interval that they both are simultaneously present in concentrations which effect substantial in vivo inhibition, preferably blocking, of their respective target proteases.

5 (currently amended). A method ~~for preventing or arresting invasive remodelling in a mammal, the method~~ according to claim 1 comprising administering, to the mammal, an effective amount of at least one third substance which, in the mammal, effects inhibition of both the in vivo protein cleaving actions of plasmin as well as of active derivatives thereof and of the in vivo protein cleaving actions of at least one metalloprotease as defined in claim 4, said at least one third substance(s) being one(s) which, upon administration in an effective amount, result(s) in a significantly higher inhibition of embryo implantation and/or wound healing in $Plg^{-/-}$ mice than in wildtype mice.

6 (original). A method according to claim 4, wherein at least one of the at least one first and/or at least one second substances is a third substance which, in the mammal, effects inhibition of both the in vivo protein cleaving actions of plasmin as well as of active derivatives thereof and of the in vivo protein cleaving actions of at least one metalloprotease as defined in claim 4, said at least one third substance(s) being one(s) which, upon administration in an effective amount, result(s) in a significantly higher inhibition of embryo implantation and/or wound healing in $Plg^{-/-}$ mice than in wildtype mice.

7 (original). A method according to claim 4, wherein the at least one first substance is administered in an amount which gives rise to a concentration which is at or below the maximum pharmacologically acceptable concentration of said first substance alone, and, when the concentration is below the maximum pharmacologically acceptable concentration of the first substance alone, said concentration is one which gives rise to substantially the same inhibition as the maximum pharmacologically acceptable concentration of the first substance alone, and the at least one second substance is administered in an amount which gives rise to a concentration which, when the second substance is administered simultaneously with or after the administration of the at least one first substance, is at or below the maximum pharmacologically acceptable concentration, and which, if below the maximum pharmacologically acceptable concentration, is a concentration which gives rise to substantially the same inhibition as the maximum pharmacologically acceptable concentration.

8 (original). A method according to claim 4, wherein the at least one second substance is administered in an amount which gives rise to a concentration which is at or below the maximum pharmacologically acceptable concentration of the second

substance alone, and, when the concentration is below the maximum pharmacologically acceptable concentration of the second substance alone, said concentration is one which gives rise to substantially the same inhibition as the maximum pharmacologically acceptable concentration of the second substance alone, and the at least one first substance is administered in an amount which gives rise to a concentration which, when the first substance is administered simultaneously with or after the administration of the second substance, is at or below the maximum pharmacologically acceptable concentration, and which, if below the maximum pharmacologically acceptable concentration, is a concentration which gives rise to substantially the same inhibition as the maximum pharmacologically acceptable concentration.

9 (original). A method according to claim 5, wherein the at least one third substance is administered in an amount which gives rise to a concentration which is at or below the maximum pharmacologically acceptable concentration of the third substance alone, and, when the concentration is below the maximum pharmacologically acceptable concentration of the third substance alone, said concentration is one which gives rise to substantially the same inhibition as the maximum pharmacologically acceptable concentration of the third substance alone.

10 (original). A method according to claim 4, wherein the first substance is administered in an amount which, when administered simultaneously with or after the administration of the second substance, gives rise to a concentration which results in substantially the same inhibition as the maximum pharmacologically acceptable concentration.

11 (original). A method according to claim 4, wherein the second substance is administered in an amount which, when administered simultaneously with or after the administration of

the first substance, gives rise to a concentration which results in substantially the same inhibition as the maximum pharmacologically acceptable concentration.

12 (original). A method according to claim 1, wherein the at least one first substance is administered in an amount of between 1 and 1000 mg per day.

13 (original). A method according to claim 1, wherein the metalloprotease is selected from the group consisting of a collagenase, a stromelysin, a gelatinase, an elastase, and a membrane type metalloprotease.

14 (original). A method according to claim 13, wherein the collagenase is selected from the group consisting of MMP-1, MMP-8, and MMP-13.

15 (original). A method according to claim 13, wherein the stromelysin is selected from the group consisting of MMP-3, MMP-7, MMP-10, and MMP-11.

16 (original). A method according to claim 13, wherein the gelatinase is selected from the group consisting of MMP-2 and MMP- 9.

17 (original). A method according to claim 13, wherein the elastase is MMP-12.

18 (original). A method according to claim 13, wherein the membrane type metalloprotease is selected from the group consisting of MMP-14, MMP-15, and MMP-16.

19 (original). A method according to claim 1, wherein the invasive remodelling is that of a malignant neoplasm.

20 (original). A method according to claim 19, wherein the malignant neoplasm is selected from the group consisting of carcinoma such as adenocarcinoma, sarcoma such as liposarcoma, fibrosarcoma, chondrosarcoma, osteosarcoma, leiomyosarcoma, rhabomyosarcoma, glioma, neuroblastoma, medullablastoma, malignant melanoma, neurofibrosarcoma, hemangiosarcoma, and lymphangiosarcoma, and other malignant neopiasms such as

malignant teratoma, dysgerminoma, seminoma, choriocarcinoma, leukemia, and lymphoma.

21 (original). A method according to claim 20, wherein the carcinoma is carcinoma of the lung, the breast, the prostate or the colon.

22 (original). A method according to claim 1 for use in contraception.

23 (original). A method according to claim 4, wherein the at least one first substance is selected from the group consisting of aprotinin, tranexamic acid, N∝-trans-4-aminomethylcyclohexane carbonyllysine 4 benzoylanilide, N∝-trans-4-aminomethylcyclohexane carbonyl-O-bromobenzyloxycarbonyltyrosine 4 acetylanilide, 1-(ethoxy-carbonyloxy)ethyl trans-4-aminomethylcyclohexanecarboxylate hydrochloride (KABI 2161), alpha-2-antiplasmin, alpha-2-makroglobulin, tumour associated trypsin inhibitor, urinary trypsin inhibitor, leupeptin, pyroglutamyl-Leu-Arg-CHO, 6-aminocaproic acid, p-aminobenzamidine, bis(5-amidino-2-benzimidazolyl)methane, alpha-N-acetyl-L-lysine methyl ester, tosyl-lysine chloromethyl ketone, and Boc-D-Phe- ProBoro-Arg-OH.

24 (original). A method according to claim 4, wherein the at least one second substance is selected from the group consisting of a tissue inhibitor of metalloproteases, alpha-2-macroglobulin, Galardin™, N-[2R-2-(hydroxamidocarbonylmethyl)-4-methylpentanolyl]-L-tryptophan methylamide, batimastat, marimastat, GI 129471, GI 168, GI 173, GI 179, GI 184, Cl-A, Cl-B, RP59794, SC-44463, Ro31-4724, CT1746, SCH 47890, a peptide hydroxamate, LMHKPRCGVPDVGG (SEQ ID NO:1), TNF-∝ releasing protease inhibitor, Zincov®, Pro-Ileu, phosphoramidon, thiorphan, tiopronin, a tetracycline, N-acetylcysteine, EDTA, and 1,10 phenanthrolene.

25 (original). A method according to claim 24, wherein the tissue inhibitor of metalloproteases is selected from the group consisting of TIMP-1, TIMP-2, and TIMP-3.

26 (original). A method according to claim 24, wherein the peptide hydroxamate is Pro-Leu-Gly-NHOH.

27 (original). A method according to claim 5, wherein the at least one third substance is selected from the group consisting of a conjugate of Galardin™ with aprotinin, a conjugate of Galardin™ with tranexamic acid, and a conjugate of Galardin with leupeptin.

28 (original). A method according to claim 1, wherein the at least one extracellular protein is selected from the group consisting of collagen, elastin, fibrin and proteoglycan.

29 (original). A method according to claim 1, wherein the at least one extracellular protein is fibronectin or laminin.

30 (original). A method according to claim 1, wherein the at least one extracellular protein is a growth factor or a cytokine, such as transforming growth factor β (TGFβ), TNF∝, basic fibroblast growth factor, and precursors of TGFβ or of other growth factors or cytokines.

31 (original). A method according to the claim 4, wherein the substances independently are administered via the parenteral (such as intravenous and intraarterially), intraperitoneal, intramuscular, subcutaneous, intradermal, oral, buccal, sublingual, nasal, rectal or transdermal route.

32 (original). A method according to claim 4, wherein the substances independently are targeted for a specific site of action.

33 (original). A method according to claim 4, wherein the substances are used systemically.

34 (original). A method for preventing or arresting invasive remodelling in a mammal, the invasive remodelling not comprising contraction of tissue or corneal ulceration, the

method comprising 1) inhibiting or abolishing, in the mammal, the in vivo protein cleaving actions of at least one first protease, A, and 2) simultaneously therewith inhibiting or abolishing the in vivo protein cleaving actions of at least one other protease, B, wherein A and B have at least one extracellular protein as a common substrate, said at least one protease, B, being essential for embryo implantation and/or wound healing and/or necessary for invasive tissue destruction associated with malignant growth in the mammal when the protein cleaving actions of A are substantially abolished in the mammal but not when the protein cleaving actions of A are substantially intact in the mammal at least one of A and B being at least one metalloprotease.

35 (original). A method according to claim 34, wherein A and B are independently of each other selected from the group consisting of metalloproteases, cysteine proteases, serine proteases and aspartic proteases, at least one of A and B being at least one metalloprotease.

36 (original). A method of screening for a substance which is capable of interfering with invasive remodelling in a mammal, including a human being, the method comprising providing an animal wherein has been substantially abolished the in vivo protein cleaving actions of at least one protease which contributes to invasive remodelling, and thereafter assessing the effect of administration of the substance to the animal on at least one process known to involve invasive remodelling, and finally establishing as a result that the substance is capable of interfering with invasive remodelling if the at least one process is inhibited to a significantly higher degree than in both the animal when it does not receive the substance and in a reference animal which has not had the in vivo protein cleaving actions of the at least one protease substantially abolished.

37 (original). A method according to claim 36, wherein the substantial abolishment of the in vivo protein cleaving actions

of the at least one protease has been accomplished by genetic modification of the animal or by pharmaceutical inhibition.

38 (original). A method according to claim 36, wherein the at least on protease is selected from the group consisting of a collagenase, a stromelysin, a gelatinase, an elastase, and a membrane type metalloprotease .

39 (original). A method according to claim 37, wherein the at least on protease is selected from the group consisting of a collagenase, a stromelysin, a gelatinase, an elastase, and a membrane type metalloprotease.